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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,417	11/16/2000	Richard Shimkets	15966-606 (Cura-106)	7720

7590 09/06/2002

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	15

DATE MAILED: 09/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/715,417	SHIMKETS ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,29,32,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *44* is/are allowed.

6)☐ Claim(s) *1,2,4,29,32 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,8,10,1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants preliminary amendment of claims 1, 2, 4, 29 and 32, cancellation of claims 3, 5-28, 30, 31 and 33-43 and the addition of new claims 44 and 45, Paper No. 14, 7/8/2002, is acknowledged Claims 1, 2, 4, 29, 32, 44 and 45 are at issue and are present for examination.

Election/Restrictions

Applicant's election without traverse of Group I, Claims 1-4, 29 and 32 in Paper No. 13 is acknowledged.

Priority

Applicants claim of priority to USSN 60/166,336, filed November 19, 1999, 60/187,844, filed March 8, 2000, and 60/167,785, filed November 29, 1999 which are each incorporated by reference in their entirety is acknowledged.

It is noted that applicants claim to priority for the invention presently being prosecuted, the polypeptide of NOV16 (SEQ ID NO: 32), is granted to provisional application number 60/187,844 and this prioity is granted for the specific protein only, not for those claims which are drawn to a broader genus of proteins then SEQ ID NO: 32, as the specific protein and its encoding nucleic acid are the only inventions disclosed in the referred to priority application.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Applicants filing of information disclosures, Paper No. 7, filed 5/1/2001, and Paper No. 8, filed 10/1/2001, Paper No. 10, filed 2/22/2002, and Paper No. 11, filed 4/22/2002, is acknowledged. Those references considered have been initialed. Those that have been lined through, reference C14 of Paper No. 8, filed 10/1/2001, "International Search Report, issued August 20, 2001" has not been considered because this citation is not sufficient to indicate which application the search report is for and the referred to search report could not be located in the file.

Specification

The disclosure is objected to because of the following informalities: On page 53, line 26, under the heading and discussion regarding "NOV 16" applicants refer to "NOV 14" as a member of the serine/threonine kinase family. While this prediction of the function of NOV 14 may be true, it is believed that applicants intended this recitation to refer to "NOV 16" not "NOV 14".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 29 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (2, 29 and 32 dependent on) is indefinite in that it is confusing in that it is drawn to a polypeptide comprising the mature form of an amino acid sequence of SEQ ID NO: 32. While applicants discuss that the "mature" form of a polypeptide or protein (in general) may arise from a step of post-translational modification including proteolytic cleavage, glycosylation, myristoylation or phosphorylation (see pages 54-55), applicants have not taught that any such "maturation" process occurs with the protein having the amino acid sequence of SEQ ID NO: 32. Thus it is unclear what the "mature" form of a polypeptide having an amino acid sequence of SEQ ID NO: 32 is and how this is different from a polypeptide comprising the sequence of SEQ ID NO: 32.

Based on the above, it is unclear how claim 1 is different from claim 44, in that they are both drawn to a polypeptide comprising an amino acid sequence of SEQ ID NO: 32.

Claim 2 is indefinite in that it is confusing in the recitation "... the polypeptide of claim 1 that is a naturally occurring allelic variant of the sequence given by SEQ ID NO: 32." This phrase is confusing because it appears that applicants are attempting to claim

a naturally occurring allelic variant of SEQ ID NO: 2, but because this claim depends from Claim 1, all of the limitations of claim 1 are read into the claim, which includes that the claim must be drawn to a polypeptide comprising the mature form of an amino acid sequence of SEQ ID NO: 2. Therefore, claim 2 appears to improperly depend from claim 1 in that it appears that claim 2 is drawn to a broader scope than claim 1 from which it depends. For the purpose of advancing prosecution, the claim is interpreted as if it did not depend upon claim 1 and is drawn to polypeptides that are naturally occurring allelic variants of the amino acid sequence of SEQ ID NO: 32.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 4 and 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2, 4 and 45 are directed to all possible polypeptides comprising a naturally occurring allelic variant of the amino acid sequence of SEQ ID NO: 32 (claim 2, and See above 112 2nd paragraph rejection), all possible polypeptides comprising an amino acid comprising one or more conservative substitutions in the amino acid sequence of SEQ ID NO: 32 (claim 4), and all possible polypeptides comprising an

amino acid sequence which is at least 95% identical to an amino acid sequence of SEQ ID NO: 32 (claim 45).

The specification, however, only provides a single representative species, the polypeptide having the amino acid sequence of SEQ ID NO: 32, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these polypeptides by any identifying structural characteristics or functional properties other than kinase activity, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Further, specification states that natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the gene (page 61, lines 5-6). Alleles may result in altered mRNAs or polypeptides whose structure or function may or may not be altered. Applicants disclosure does not provide any specific information about the structure of naturally occurring (alleles) variants of SEQ ID NO: 32 (i.e. where are the regions within which mutations are likely to occur) nor discloses any function for naturally occurring variants. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO:32 relates to the structure of any naturally occurring alleles. The general knowledge in the art concerning alleles does not provide any indication of how one allele is representative of

unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art structure of one does not provide guidance to the structure of others. The genus of polypeptides that comprise the claimed polypeptides is a large variable genus. Therefore, many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus (i. e the sequence of SEQ ID NO: 32) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 2, 4 and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising an amino acid sequence which is at least 95% identical to an amino acid sequence of SEQ ID NO: 32, wherein said polypeptide has kinase activity, does not reasonably provide enablement for any polypeptide comprising an amino acid sequence which is at least 95% identical to an amino acid sequence of SEQ ID NO: 32 or any polypeptide comprising any number of conservative substitutions of SEQ ID NO: 32. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 2, 4 and 45 are directed to all possible polypeptides comprising a naturally occurring allelic variant of the amino acid sequence of SEQ ID NO: 32 (claim 2, and See above 112 2nd paragraph rejection), all possible polypeptides comprising an amino acid sequence comprising one or more conservative substitutions in the amino acid sequence of SEQ ID NO: 32 (claim 4), and all possible polypeptides comprising an amino acid sequence which is at least 95% identical to an amino acid sequence of SEQ ID NO: 32 (claim 45).

Claims 2, 4 and 45 are so broad as to encompass any polypeptide comprising a naturally occurring allelic variant of the amino acid sequence of SEQ ID NO: 32 (claim 2, and See above 112 2nd paragraph rejection), one or more conservative substitutions in the amino acid sequence of SEQ ID NO: 32 (claim 4), and an amino acid sequence which is at least 95% identical to an amino acid sequence of SEQ ID NO: 32 (claim 45).

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place structural limits (claims 2 and 4) but absolutely no functional limits (claims 2, 4 and 45) on the claimed polypeptides. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that polypeptide comprising the amino acid sequence of SEQ ID NO: 32, wherein said polypeptide has kinase activity.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all polypeptides with the claimed relationship to SEQ ID NO: 32 (i.e. allelic variants, including conservative substitutions and 95% amino acid sequence identity) because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the desired activity; (B) the general tolerance of the claimed polypeptides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of the polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired biological activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus.

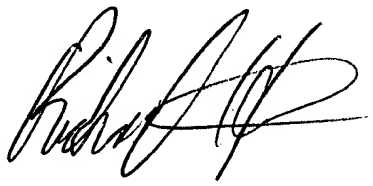
Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polypeptide comprising the claimed variations of SEQ ID NO: 32. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
September 6, 2002